TABLE 1. Psychiatric Conditions Related to Convulsive Events

Presentation	Clinical Features
Preictal dysphoria	Depressive symptoms or irritability occur days before a convulsive episode and are relieved by the seizure.
Ictal psychosis	Psychotic symptoms are a direct reflection of ictal activity. It is characterized by the fluctuation of the level of consciousness with psychotic symptoms. Episodic amnesia is associated.
Postictal delirium	Sudden confusion with agitation lasts up to half an hour after a seizure, with spontaneous resolution. Hallucinations are common.
Postictal psychosis	1) Psychotic episode within the first week after last seizure. 2) Psychotic symptoms last >15 h and <2 mo. 3) Presence of hallucinations, delusions, disorganized behavior, formal thought disorders, or affective changes. 4) There is no evidence of intoxication, nonconvulsive epileptic status, recent head trauma, intoxication or withdrawal effect of any substance (especially alcohol), or prior psychotic disorders. *The presence of a lucid interval (usually approximately 24–48 h) between the last seizure and onset of psychotic symptoms distinguishes postictal psychosis from a postictal delirium.
Interictal psychosis	1) Hallucinations, delusions, or disorganized behavior without temporal relationship with the convulsive events. 2) First psychotic episode after the onset of epileptic disease. 3) Duration of at least 24 h in a state of clear consciousness.

observed in bipolar disorder, both in monotherapy[10] and in combination.[11] The fact that the effects of this drug are so poorly understood reflects a need to further investigate the clinical and biological factors pointing to an association between levetiracetam and affective syndromes. In our case, before the full manic syndrome with psychotic features was established, our patient presented with affective-mixed symptoms such as dysphoria, irritability, mood lability, and aggressiveness. Most levetiracetam-associated manic/psychotic episodes reported in the literature were preceded by irritability,[2–5] mood lability,[2,4] aggressiveness, and psychomotor agitation.[2] This affective-mixed symptoms complex may be a prodromal marker of subsequent severe manic/psychotic episodes.[12,13] Therefore, when levetiracetam titration is started, these symptoms should be carefully monitored and promptly treated to avoid a progression to manic/psychotic episodes. Some studies have hypothesized that the pathophysiology underlying levetiracetam-related mania may be due to levetiracetam's antagonism of N-type calcium channels and α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptors.[14]

AUTHOR DISCLOSURE INFORMATION

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REFERENCES

1. Chen B, Choi H, Hirsch LJ, et al. Psychiatric and behavioral side effects of antiepileptic drugs in adults with epilepsy. *Epilepsy Behav.* 2017; 76:24–31. doi:10.1016/j.yebeh.2017.08.039.
2. Park EM, Holmes JA, Reeder-Hayes KE. Acute mania associated with levetiracetam treatment. *Psychosomatics*. 2014;55:98–100. doi:10.1016/J.PSYM.2013.06.008.
3. Ozcan H, Ulkevan T, Fatih Ustundag M, et al. Levetiracetam-induced acute mania. *Bull Clin Psychopharmacol*. 2015;25:320. doi:10.5455/bcp.20150212042745.
4. Altınöz AE, Tosun Altınöz Ş, Güzel Biltekin B, et al. Levetiracetam induced hypomania: a case report. *Ther Adv drug Saf*. 2019;10:1–4. doi:10.1177/2042098619876754.
5. Fonseca JB, Rodrigues R, Lourenço E, et al. Levetiracetam induced mania—a case report. *Rev Psiquiatr Clin*. 2020;47:30. doi:10.1590/0101-60830000000226.
6. Chen Z, Lusicic A, O'Brien T, et al. Psychotic disorders induced by antiepileptic drugs in people with epilepsy. *Brain*. 2016;139:2668–2678. doi:10.1093/BRAIN/AWW196.
7. Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther.* 1981;30: 239–245. doi:10.1038/clpt.1981.154.
8. Kanner AM, Rivas-Grajales AM. Psychosis of epilepsy: a multifaceted neuropsychiatric disorder. *CNS Spectr.* 2016;21:247–257. doi:10.1017/S1092852916000250.
9. Lamberty Y, Margineanu DG, Klitgaard H. Effect of the new antiepileptic drug Levetiracetam in an animal model of mania. *Epilepsy Behav.* 2001;2:454–459. doi:10.1006/EBEH.2001.0254.
10. Kaufman KR. Monotherapy treatment of bipolar disorder with levetiracetam. *Epilepsy Behav.* 2004;5:1017–1020. doi:10.1016/J.YEBEH.2004.08.009.
11. Bräunig P, Krüger S. Levetiracetam in the treatment of rapid cycling bipolar disorder. *J Psychopharmacol*. 2003;17:239–241. doi:10.1177/0269881103017002015.
12. Hansen CC, Ljung H, Brodtkorb E, et al. Mechanisms underlying aggressive behavior induced by antiepileptic drugs: focus on topiramate, levetiracetam, and perampanel. *Behav Neurol.* 2018;2018:1–18. doi:10.1155/2018/2064027.
13. Pinckaers FME, Boon ME, Majoie MHJM. Risk factors predisposing to psychotic symptoms during levetiracetam therapy: a retrospective study. *Epilepsy Behav.* 2019;100:106344. doi:10.1016/J.YEBEH.2019.05.039.
14. Steinhoff BJ, Staack AM. Levetiracetam and brivaracetam: a review of evidence from clinical trials and clinical experience. *Ther Adv Neurol Disord*. 2019;12:1–23. doi:10.1177/1756286419873518.

Elevated Clozapine Blood Concentrations After Second COVID-19 Vaccination With Spikevax (COVID-19 Vaccine Moderna)

To the Editors:

It is already known that coronavirus disease 2019 (COVID-19) and other inflammatory diseases can lead to elevated clozapine blood concentrations.[1–4] In these conditions,

therapeutic drug monitoring of clozapine[5] may help maintain clozapine drug concentrations within the therapeutic reference range, as adequate dose titration of clozapine during infectious diseases can prevent serious adverse drug reactions and intoxication.

Various studies have been published, reporting about inflammation-mediated changes in drug metabolism.[6–8] The decrease in expression and activity of cytochrome P450 (CYP) enzymes is primarily induced by a transcriptional suppression of the respective CYP mRNAs and can be selective for a distinct isoform of CYP and be dependent on the respective pathophysiology of inflammation.[6,9–11] The CYP isoenzymes CYP1A2 and CYP2C19 are the major enzymes involved in drug metabolism of clozapine.[5]

In March 2021, Thompson et al[12] reported about a case of elevated clozapine levels after first administration of a Pfizer-BioNTech mRNA vaccine. To date, no reports about elevated clozapine blood concentrations have been published for non–mRNA-based vaccines. Raaska et al[13] found that influenza vaccine does not affect clozapine serum concentrations. We report about a case of increased clozapine blood concentrations after second COVID-19 vaccination with Spikevax (COVID-19 Vaccine Moderna).

Written consent for publication had been obtained from the following case.

CASE REPORT

A 42-year-old man (born in Eritrea) with diagnosis of paranoid schizophrenia (F20.0) was admitted in December 2019 in the forensic psychiatric hospital in Riedstadt. He had no further comorbidities and smoked 5 cigarettes per day, which was controlled by the nursing staff. Therefore, the access of the patient to cigarettes, and the number of cigarettes smoked per day, was consistent through the period before and after the first and second vaccination. The patient had no history of COVID-19 before immunization and was not febrile at any time. He was tested for COVID-19 two times (September 18, 2020 COVID-19 rapid test, December 07, 2020 COVID-19 PCR test). He did not leave the clinic for free time activities. In April 2021, he received the first COVID-19 vaccination with Spikevax (COVID-19 Vaccine Moderna) without noticeable problems. Prothipendyl (80 mg), haloperidol (8 mg), and lorazepam (2 mg) were prescribed during this time. Because of nonresponse to several antipsychotic drugs, clozapine therapy was started in May 2021, in combination with haloperidol and lorazepam. Seven days later, the patient already received 100-mg clozapine, and the second COVID-19 vaccination was conducted. At this time and during the next 12 days, comedication was haloperidol (8 mg) and lorazepam (1 mg). Clozapine blood concentration was measured under trough-level conditions, considering that steady state conditions[5] requiring 3 to 4 days at the same dose (4–5 half-lives) were not present during dose escalation (Table 1). Clozapine concentration at the day of vaccination was 270 ng/mL and, therefore, below the therapeutic reference range (Table 1).[5] As the clozapine concentration was measured with a Saladax MyCare Insite Analyzer laboratory photometer, requiring only a single drop of blood from a finger stick (assay performance validated according to the US Food and Drug Administration and In Vitro Diagnostic Directive standards), measuring of norclozapine was not possible. One day after the vaccination, the patient appeared

TABLE 1. Clozapine Dosage, Blood Concentration, Concentration to Dose Ratio (C/D), and Adverse Drug Reactions With the Passage of Time and Laboratory Measures

Date	Clozapine Dosage, mg	Clozapine Blood Concentration, ng/mL	C/D, ng/mL/mg	Comment
April 13, 2021	**First COVID-19 vaccination with Spikevax (COVID-19 Vaccine Moderna)**			
May 18, 2021	**Beginning clozapine therapy with 12.5 mg**			
May 25, 2021	**Second COVID-19 vaccination with Spikevax (COVID-19 Vaccine Moderna)**			
	100	270	2.7	Steady state not reached; patient is agitated since May 26, 2021, constantly leaves his room day and night
May 30, 2021	175	868	4.96	Steady state not reached; dizziness, gait disturbances and drowsiness, as well as disorientation to place and time, consistent with delirium, tachycardia, and hypotension (19:10 o'clock: arterial blood pressure 96/64, pulse 112)
May 31, 2021	Clozapine paused	452		
June 1, 2021	50	246	4.92	Steady state not reached; ECG in normal condition
June 4, 2021	150	282	1.88	Steady state not reached
June 06, 2021	200	391	1.96	Steady state not reached
June 10, 2021	**Results of genotyping present**			
June 29, 2021	112.5	336	2.99	Steady state reached

Date	Leukocytes, $10^3/\mu L$	Neutrophils, %	Monocytes, %	Lymphocytes, %	Eosinophils, %	CRP, mg/L	GOT/AST, U/L	GPT, U/L	γ-GT, U/L	GFR, mL/min
Reference range	3.9–10.2	42–77	2–10	20–44	1–5	<0.5	<50	<50	<60	>100
May 12, 2021	5.8	36.4	7.2	45.9	8.8	<0.5	27	50	65	86.1
May 25, 2021	5.4	46.9	6.9	36.7	8.0	6	30	52	71	106.5
Second COVID-19 vaccination with Spikevax (COVID-19 Vaccine Moderna)										
June 01, 2021	5.4	46.2	7.2	37.6	8.1	18	28	64	115	105.1
June 08, 2021	6.5	44.2	7.5	40.0	6.9	10	38	56	89	95.9
June 29, 2021	6.2	37.8	6.3	45.2	9.3	<0.5	24	37	64	102.3

ECG, electrocardiogram; GFR, glomerular filtration rate; GPT, glutamate-pyruvate transaminase; GT, glutamyl transferase; GOT/AST, glutamic oxaloacetic transaminase/aspartate aminotransferase.

agitated and constantly left his room at daytime and at night. Five days after vaccination, the patient received 175-mg clozapine, and agitation became worse (Table 1). In addition, dizziness, gait disturbances, drowsiness, as well as disorientation to place and time, consistent with delirium, occurred. The patient had hypotension (arterial blood pressure 96/64) and tachycardia (pulse 112). The clozapine blood level was measured and attested that the patient was 868 ng/mL above the therapeutic reference range.[5] Therefore, clozapine therapy was paused, and the blood level decreased in line with the clozapine half-life[5] to 452 ng/mL 1 day later (Table 1). The neurological symptoms had resolved, and the patient's mental state was at the prevaccination baseline.

Ten days after vaccination, concentration-to-dose ratio (C/D, in nanograms per milliliter per milligram) decreased enormously, but steady state was still not given. Over a month after vaccination, the C/D was 2.99 under steady-state conditions (Table 1), and the patient remained clinically stable.

As the patient was, also before the second vaccination, above the clozapine dose-related reference range with a C/D of 2.7 (Table 1; ordinary range, 0.21–0.79[5]) and born in Eritrea (genetic diversity is greater in Africa than in other continental populations[14]), a CYP genotyping was conducted. A CYP2C19 intermediate metabolizer status was detected that could explain the increased C/D.

Leucocytes, neutrophils, monocytes, and lymphocytes were without noticeable problems also after the second vaccination (Table 1), eosinophils were above the ordinary range (possibly due to an allergic reaction). C-reactive protein (CRP) was slightly increased at the day and for weeks after the second vaccination (6–18 mg/L; Table 1) without signs of a bacterial/viral infection. Glutamate-pyruvate transaminase and γ-glutamyl transferase were slightly above the therapeutic range.

DISCUSSION

There was a close temporal relation between serum level increase of clozapine and the second vaccination with Spikevax in the patient. Because pharmacokinetic drug-drug interactions due to comedication were not identified and smoking status did not change, it seemed likely that the increase in drug serum concentration (C/D) was associated with the second vaccination. Cytochrome P450 genotype of the patient did not explain the increase in C/D.

Bayraktar et al[15] examined the potential interaction between clozapine and COVID-19 vaccines from different perspectives. They indicated that mRNA COVID-19 vaccines brought out strong $CD4^+$ and $CD8^+$ T-cell and antibody responses that led to the production of cytokines, especially interferon γ. Interferon γ could lead to decreased expression of CYP enzymes. Bayraktar et al[15] concluded that COVID-19 vaccines have strong antibody responses, and this would lead to potential interactions with some drugs as well as clozapine. Moreover, Kow and Hasan[16] published a letter about potential interactions between COVID-19 vaccines and antiepileptic drugs. The authors also indicated that administration of the COVID-19 mRNA vaccinations elicited strong antibody responses with a high fraction of specific T cells producing interferon γ, which could lead to reduced expression of CYP1A2 and CYP3A4, which are involved in clozapine metabolism. Nevertheless, T-cell responses with the production of interferon γ are not specific to mRNA vaccines.

C-reactive protein increase after the second vaccination with Spikevax (COVID-19 Vaccine Moderna) and the clozapine level increase was much lower in the prescribed patient, compared with the increase in the predisposed patient after the first Pfizer-BioNTech vaccination in the case report of Thompson et al.[12] A more severe drug increase (perhaps due to higher interferon γ concentration) could have been possible if clozapine would have been administered before the first vaccination. Furthermore, the described patient had no comorbidities or any predisposing conditions, compared with the patient of Thompson et al.[12] Adverse events began on the fourth day after vaccination in the report of Thompson et al,[12] similar to this report after 5 days.

Unfortunately, in this case, CRP values were only measured at the day of second vaccination and then 7 days later. Perhaps, the peak elevation of CRP was earlier than day 7.

Clozapine blood concentrations are highly sensitive to inflammation-related inhibition of especially CYP1A2 activity,[4,17] but the underlying multifactorial mechanisms are incompletely understood. A vaccination-induced activation of proinflammatory cytokines and after impairment of hepatic CYP450 synthesis may be a reason of the increased serum levels, but alterations of drug transporters and other drug-metabolizing enzymes could have been affected with corresponding consequences for drug metabolism and excretion.[6,11,18,19] As various reasons may have led to the increased C/D of clozapine after vaccination, this single case report cannot prove a causal relationship between mRNA vaccination and the elevation of clozapine blood concentrations, but caution is required. Nevertheless, the high C/D ratios were consistent with inhibition of CYP1A2 and CYP2C19 metabolism.

During the COVID-19 pandemic, therapeutic drug monitoring should be conducted in patients treated with clozapine that receive a first or second mRNA vaccination, as dose adaptation can be necessary in case of adverse effects. At the time of vaccination, instructions to the patient and caregivers to watch for changes in symptoms over the first week after vaccination is recommended. If symptoms occur, seeking medical attention and obtaining a complete blood count/differential, CRP and clozapine level would be advisable, as well as any other assessment and intervention depending on the individual case. Moreover, it has to be considered that dose adaptation may also be necessary after a few days of dose reduction to avoid loss of sufficient antipsychotic drug action.

We emphasize that (1) patients on clozapine ought to be a high priority for vaccination, (2) the results reported do not imply that treatment with clozapine is a contraindication to vaccination, and (3) the results do not imply that clozapine should not be initiated in vaccinated patients.

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REFERENCES

1. Tio N, Schulte PFJ, Martens HJM. Clozapine intoxication in COVID-19. *Am J Psychiatry*. 2021;178:123–127. doi:10.1176/appi.ajp.2020.20071039.
2. Cranshaw T, Harikumar T. COVID-19 infection may cause clozapine intoxication: case report and discussion. *Schizophr Bull*. 2020;46:751. doi:10.1093/schbul/sbaa070.
3. Dotson S, Hartvigsen N, Wesner T, et al. Clozapine toxicity in the setting of COVID-19. *Psychosomatics*. 2020;61:577–578. doi:10.1016/j.psym.2020.05.025.
4. Hefner G, Shams ME, Unterecker S, et al. Inflammation and psychotropic drugs: the relationship between C-reactive protein and antipsychotic drug levels. *Psychopharmacology (Berl)*. 2016;233:1695–1705. doi:10.1007/s00213-015-3976-0.
5. Hiemke C, Bergemann N, Clement HW, et al. Consensus guidelines for therapeutic drug monitoring in neuropsychopharmacology: update 2017. *Pharmacopsychiatry*. 2018;51:9–62. doi:10.1055/s-0043-116492.
6. Aitken AE, Richardson TA, Morgan ET. Regulation of drug-metabolizing enzymes and

transporters in inflammation. *Annu Rev Pharmacol Toxicol*. 2006;46:123–149. doi:10.1146/annurev.pharmtox.46.120604.141059.

7. Petrovic V, Teng S, Piquette-Miller M. Regulation of drug transporters during infection and inflammation. *Mol Interv*. 2007;7:99–111. doi:10.1124/mi.7.2.10.
8. Renton KW, Knickle LC. Regulation of hepatic cytochrome P-450 during infectious disease. *Can J Physiol Pharmacol*. 1990;68:777–781.
9. Iber H, Sewer MB, Barclay TB, et al. Modulation of drug metabolism in infectious and inflammatory diseases. *Drug Metab Rev*. 1999;31:29–41. doi:10.1081/dmr-100101906.
10. Morgan ET. Regulation of cytochrome p450 by inflammatory mediators: why and how? *Drug Metab Dispos*. 2001;29:207–212.
11. Renton KW. Alteration of drug biotransformation and elimination during infection and inflammation. *Pharmacol Ther*. 2001;92:147–163.
12. Thompson D, Delorme CM, White RF, et al. Elevated clozapine levels and toxic effects after SARS-CoV-2 vaccination. *J Psychiatry Neurosci*. 2021;46:E210–e211. doi:10.1503/jpn.210027.
13. Raaska K, Raitasuo V, Neuvonen PJ. Effect of influenza vaccination on serum clozapine and its main metabolite concentrations in patients with schizophrenia. *Eur J Clin Pharmacol*. 2001;57:705–708. doi:10.1007/s002280100375.
14. Rajman I, Knapp L, Morgan T, et al. African genetic diversity: implications for cytochrome P450-mediated drug metabolism and drug development. *EBioMedicine*. 2017;17:67–74. doi:10.1016/j.ebiom.2017.02.017.
15. Bayraktar İ, Yalçın N, Demirkan K. The potential interaction between COVID-19 vaccines and clozapine: a novel approach for clinical trials. *Int J Clin Pract*. 2021;75:e14441. doi:10.1111/ijcp.14441.
16. Kow CS, Hasan SS. Potential interactions between COVID-19 vaccines and antiepileptic drugs. *Seizure*. 2021;86:80–81. doi:10.1016/j.seizure.2021.01.021.
17. Moschny N, Hefner G, Grohmann R, et al. Therapeutic drug monitoring of second- and third-generation antipsychotic drugs-influence of smoking behavior and inflammation on pharmacokinetics. *Pharmaceuticals (Basel)*. 2021;14. doi:10.3390/ph14060514.
18. Morgan ET, Goralski KB, Piquette-Miller M, et al. Regulation of drug-metabolizing enzymes and transporters in infection, inflammation, and cancer. *Drug Metab Dispos*. 2008;36:205–216. doi:10.1124/dmd.107.018747.
19. Renton KW. Regulation of drug metabolism and disposition during inflammation and infection. *Expert Opin Drug Metab Toxicol*. 2005;1:629–640. doi:10.1517/17425255.1.4.629.

Topiramate-Associated Acute Bilateral Angle-Closure Glaucoma

To the Editors:

Topiramate is a sulfa derivative antiepileptic drug with a narrow range of approved uses, specifically: epilepsy monotherapy or adjunctive therapy for partial-onset seizures, primary generalized tonic-clonic seizures and seizures associated with Lennox-Gastaut syndrome, and also as prophylaxis of migraine in adults. However, because of the increasing evidence, based on controlled studies, topiramate has progressively been used in the treatment of many psychiatric conditions, namely, depression, weight loss and obesity, alcohol and drug dependence, eating disorders, post-traumatic stress disorder, and anger and aggressive behavior.[1]

Antiepileptic medications share neurochemical effects with alcohol by inhibiting neuronal excitation. The supposed efficacy of topiramate in the treatment of alcohol dependence is based on reversing chronic changes induced by alcohol resulting in dopamine-facilitated neurotransmission in the midbrain.[1]

Numerous adverse drug reactions have been associated with the use of topiramate, including acute myopia and secondary angle-closure glaucoma (ACG); metabolic acidosis; oligohidrosis and hyperthermia; hyperammonemia and encephalopathy; fetal toxicity; kidney stones; cognitive dysfunction; and psychiatric/behavioral disturbances with somnolence, fatigue and mood problems.[2]

Concerning the ocular adverse effects of topiramate, acute ACG (due to choroidal effusion and resulting anterior displacement of the lens-iris complex) is a harmful condition; patients present with ocular pain, blurred vision, headache, nausea, and vomiting. Optic nerve damage with visual field defect and vision impairment may happen if elevated intraocular pressure is persistent.[3] Although drug-associated bilateral acute ACG is a rare side effect, topiramate is commonly prescribed by psychiatrists; therefore, with the growing *off label* use of this drug, it is important to raise awareness among physicians about its potentially blinding side effect.

CASE REPORT

A 45-year-old White man with a history of alcohol abuse, presented to the emergency department (ED) with sudden onset of blurred vision in both eyes for 24 hours associated with eye pain and ocular hyperemia.

He had a medical history of alcoholic hepatitis, hyperlipidemia, and hypertension and was admitted 3 weeks before in a psychiatric ward under alcohol dependence treatment. The patient presented a history of alcohol abuse since he was 28 years old, with periods of remission and abstinence, exhibiting increased alcohol intake in the last 9 months. During this institutionalization, after an initial period on high doses of oxazepam (45 mg daily) to avoid withdrawal symptoms, topiramate 50 mg daily was initiated and raised from 50 mg to 100 mg/daily 2 days after. Within 3 days after initiating topiramate, the patient presented the above symptoms. His medications at that time also included fluoxetine 20 mg, oxazepam 15 mg, furosemide 20 mg, spironolactone 25 mg, and pantoprazole 40 mg, which he had been doing for almost 3 months. He reported no known medical allergy. He had no other relevant medical or previous ocular history, as well as no family ophthalmic history.

On the presentation to the ED his vision was 1/10 in each eye, and intraocular pressure (IOP) was 56 mm Hg right eye and 57 mm Hg left eye. Ocular examination revealed clear corneas, characteristically bilateral shallow anterior chamber and conjunctival hyperemia. Therefore, pilocarpine, timolol, and dorzolamide drops, and oral acetazolamide 250 mg were given. Laboratory test results revealed only increased parameters of alcohol misuse, namely gamma-glutamyltranspeptidase, 276 UI/L (normal value, <55 UI/L) and total bilirubin, 2.8 mg/dL (normal value, 0.2–1.2 mg/dL). Since on reexamination, IOP was 55 mm Hg on both eyes, mannitol 250 mL IV was initiated. Drug-associated ACG was highly suspected based on the finding of shallow anterior chamber and later confirmed by gonioscopy in a patient under topiramate. Thus, topiramate was discontinued, and he was admitted in the ophthalmic inpatient care for further evaluation and management. Therapy was initiated with timolol, brimonidine, and dorzolamide 2 times daily, and dexamethasone 6 times daily. Within 3 days, the signs and symptoms were relieved. At a follow-up appointment, 20 days later, the patient's vision returned to baseline. A written consent was obtained from the patient to publish the case report.

DISCUSSION

Acute bilateral secondary ACG has been frequently reported as a side effect of many medications, most often topiramate.[4] Shortly after initiating the medication or increasing the dose, patients typically present with headache, vomiting, ocular hyperemia, and sudden onset of vision changes.[5] This clinical presentation should be a red flag to the physician to tell the patient to stop the drug